prefer terminology different from "test system" she is encouraged to contact the undersigned.

Rejections under 35 U.S.C. 112

Claim 1, step (a) is rejected as vague and indefinite with respect to the term "distinguishable characteristic that is independent of the coatings". Applicants respectfully disagree that the claim is either vague or indefinite based on this term.

In this process of this invention, as in many multiplex assays, groups of particles that are differentiable by some parameter are separately treated ("coated") with different substances. In the claimed process this parameter is one that renders the subgroups of particles distinguishable from each other by a characteristic that is distinguishable by flow cytometry. Particle size is one such characteristic, and is independent of the coating that is applied to the particles. Other flow cytometry distinguishable characteristics are mentioned in the specification, for instance the inclusion of different chromophores in different subgroups of particles. In the present process the "coatings" are the substances indicated in the claims with respect to groups of particles (i) - (iv). Simultaneous (multiplex) analyte determination, as required by the claims, is carried out by flow cytometry, through which the different subgroups of particles are recognized by their flow cytometry distinguishable characteristic.

Applicants submit that the claim language is neither vague nor indefinite.

Claim 1, step (c) is held vague and indefinite because it is unclear how the label binds specifically to the particle. However, it long has been a rule that the purpose of the claims is to define what the invention is, not how it is carried out. See, e.g., In re Alul, 175 USPQ 700. The claims define that invention. Claim 1 has been amended to include the term that the labeled binding members are capable of binding to the recovered particles. However, that simply states the implicit function of the labeled binding members and is not considered in any way to limit the scope of the claim.

In fact, the various labeled binding members will bind to various coated particle in different ways because, as discussed in the specification, step (c) entails a combination of sandwich assays and competitive binding assays.

Claim 12 is rejected as ambiguous regarding the term "said particles incorporate dyes". This claim has been amended to state that the particles "include" dyes. Such broad terminology is justified, as the specification, for instance at pp. 16-17, discloses that the dyes may be included in or associated with the particles in a number of ways such as by being in a surface coating, by being embedded in the particle, by being bound to the particle molecules, etc. This amendment, however, is not deemed to affect the scope of the claims in any way.

Claim 20 is said to be indefinite in reciting "useful". This terminology has been deleted from this claim as well as from claims 21 and 22; no change in scope of these claims has been effected thereby.

The claims stand rejected as unpatentable over Watkins et al., US patent 6,280,618, in view of various secondary references. However, as stated previously, Watkins et al. is not prior art to this application. At this time this invention was made, it and the Watkins et al. patent were owned by or subject to an assignment to the same assignee, namely the present assignee Bio-Rad Laboratories, Inc. Withdrawal of all the obviousness rejections is respectfully requested.

Finally, claims 1-19 are rejected for obviousness-type double patenting over claims 1-20 of the Watkins et al. patent, above, in view of Dietzen, and further in view of Weckermann and Smith et al.

Applicants respectfully disagree that the claims are obvious from this combination of references. However, to expedite prosecution, Applicants submit herewith a terminal disclaimer with respect to the Watkins et al. patent, which should obviate this rejection.

Withdrawal of the double patenting rejection is respectfully requested.

CONCLUSION

/In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Joel G. Ackerman
Reg. No. 24,307

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
JA:ja

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Amend claims 1, 12, 20, 21 and 22 without prejudice to read:

1. (twice amended) A method for analyzing a single patient sample to simultaneously determine levels of thyroid stimulating hormone, triiodothyronine, thyroxine, and thyroid peroxidase, as a collective indication of thyroid disorders, said method comprising:

(d) incubating said sample with a mixture of particles in a first suspension, said mixture of particles comprised of groups (i) through (iv):

(v) particles coated with anti-thyroid stimulating hormone,

(vi) particles coated with anti-triiodothyronine,

(vii) particles coated with anti-thyroxine, and

(viii) particles coated with a mixture of a diluting agent and a member selected from the group consisting of thyroid peroxidase and anti-human IgG,

the particles of each group distinguishable from the particles of each other group by a flow cytometry distinguishable characteristic that is independent of the coatings of subparagraphs (i), (ii), (iii), and (iv);

(e) recovering said particles from said first suspension, and incubating said recovered particles with a mixture of labeled binding members capable of binding to the recovered particles in a second suspension, said mixture of labeled binding members comprising:

(4) labeled anti-thyroid stimulating hormone,

(5) a labeled analog composition toward which anti-triiodothyronine and anti-thyroxine have immunological binding affinity, but in which said immunological binding affinity is less than that of anti-triiodothyronine toward triiodothyronine and of anti-thyroxine toward thyroxine, and

(6) either labeled anti-human IgG when particles of group (iv) are coated with thyroid peroxidase, or labeled thyroid peroxidase when particles of group (iv) are coated with anti-human IgG;

said diluting agent being inert toward said biological markers and said labeled binding members; and

(f) recovering said particles from said second suspension and detecting the amount of label bound to said particles thus recovered from said second suspension while correlating by flow cytometry the amount of label thus detected to the group to which said label is bound, thereby simultaneously obtaining values individually representative of the levels of thyroid stimulating hormone, triiodothyronine, thyroxine, and anti-thyroid peroxidase.

12. (Amended) A method in accordance with claim 1 in which said particles [incorporate] include dyes, each of groups (i) through (iv) [incorporating]

including a distinct dye that is distinguishable by flow cytometry over the dyes of each other group, and step (c) comprises distinguishing such dyes by flow cytometry while detecting the amount of label bound to said particles.

20. (Amended) A method in accordance with claim 1 in which group (i) is comprised of two subgroups differing from each other by particle size such that one subgroup provides a substantially greater sensitivity [and is thereby useful] for measuring lower concentrations of TSH, than the other.

21. (Amended) A method in accordance with claim 1 in which group (i) is comprised of two subgroups differing from each other by coating density of anti-thyroid stimulating hormone such that one subgroup provides a substantially greater sensitivity [and is thereby useful] for measuring lower concentrations of TSH, than the other.

22. (Amended) A method in accordance with claim 1 in which group (i) is comprised of two subgroups differing from each other by both particle size and coating density of anti-thyroid stimulating hormone such that one subgroup provides a substantially greater sensitivity [and is thereby useful] for measuring lower concentrations of TSH, than the other.